



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

HARDY et al

Serial No.: 10/539,210

Filed: 6<sup>th</sup> February, 2006

Confirmation No. 2342

Group Art Unit: 1626

Title: Process for the Preparation of Phosphitylation Agents

DECLARATION OF SATYA KUCHIMANCHI

Honorable Commissioner of  
Patents and Trademarks  
Washington, D.C. 20231

Sir:

I, Satya Kuchimanchi, declare as follows:

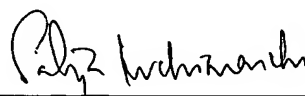
1. I am an Associate Director in the Process Development Group of Avecia Biotechnology Inc (hereafter "Avecia") in Milford, Massachusetts. My duties include research and development in the field of oligonucleotide manufacturing. I have been employed in my current position since 2006. Prior to that, from 2002 to 2006 I was employed as Group leader in Avecia Biotechnology's Process Development Group. From 2001 to 2002, I was employed by OriGenix as Principal Scientist. My duties included research and development to develop nucleoside and oligonucleotide based anti-viral therapeutics.
2. My academic qualifications are, Ph.D in organic chemistry (1987, Osmania University, Hyderabad, India); Post doctoral research at Indian Institute of Technology, Kanpur, India (1987-1989), University of Montpellier, France (1989-91) and Vanderbilt University, Nashville, TN, USA (1991-1995). I am the author or co-author of four journal articles and ten presentations all in the field of oligonucleotide chemistry.
3. I am the inventor or co-inventor of US patent application number 10/264,313 entitled "Attachment of thiophosphate tethered oligonucleotides to a solid surface", US patent application number 11/578,961 entitled "Process for the Removal of Exocyclic Base Protecting Groups" and International patent application number

PCT/GB2006/004324 entitled "Process for the Preparation of Poly(alkoxylated) Oligonucleotides"

4. I have read and understood the disclosure of JP62-212395 ("395") concerning the preparation of phosphorus amide compounds, the solvents employed and the results achieved. I have also read the subject U.S. Application No. 10/539,210 and understand the nature of the invention described and claimed therein and the results achieved.

5. Example 3 of 395 employs ether as solvent in both steps of a two-step synthesis of betacyanoethoxy bis(N,N-diisopropylamino) phosphine. The yield obtained is stated to be 42%. Example 1 of U.S. Application No. 10/539,210 employs toluene, a hydrocarbon, as solvent in both steps of a two-step synthesis of betacyanoethoxy bis(N,N-diisopropylamino) phosphine. The yield obtained is 53% by calculation from the isolated amount of product quoted. I am aware that the reaction conditions employed in 395 and U.S. Application No. 10/539,210 are not identical. Nevertheless, I believe that the reaction conditions are comparable in the context of the different nature of the solvents employed, and especially the low boiling point of ether. In my opinion, the improvement in yield achieved using the process according to U.S. Application No. 10/539,210 is attributable to the use of a hydrocarbon solvent. Furthermore, in view of the generally similar nature of hydrocarbon solvents arising from, for example, the lack of electronic or inductive effects associated with hydrocarbon solvents, in my opinion similar surprisingly improved results to those obtained with toluene would reasonably be expected for alternative hydrocarbon solvents. Accordingly, the 25% improvement in yield compared with the process of 395 represents an entirely unexpected and significant improvement arising from the use the process according to the claims of U.S. Application No. 10/539,210.

6. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both under § 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardize the validity of the application or any patent issuing thereon.



Satya Kuchimanchi

Date: 1.23.08